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The independent and joint associations of weightlifting and aerobic activity with all-cause, cardiovascular disease and cancer mortality in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial

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Abstract

Objectives: Both aerobic moderate-vigorous physical activity (MVPA) and muscle-strengthening exercise (MSE) are recommended, but the mortality benefits regarding weightlifting, a specific type of MSE, is limited. We examined the association between weightlifting, and all-cause mortality, cardiovascular-disease (CVD) and cancer mortality.

Methods: In the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, we used Cox proportional hazards regression to calculate hazard ratios (HR) and 95% confidence intervals [CI] for the associations between weightlifting and mortality, adjusting for demographic, lifestyle, and behavioral risk factors. The sample included 99,713 adults who completed the follow-up questionnaire that assessed weightlifting who were subsequently followed for mortality through 2016 (median 9, interquartile range (IQR) 7.6–10.6 years).

Results: Mean age at follow-up questionnaire was 71.3 (IQR 66–76) years, 52.6% female, with mean body mass index (BMI) of 27.8 (SD 4.9) kg/m^2. Weightlifting was associated with a 9% lower risk of all-cause mortality (HR=0.91 [95% CI:0.88–0.94]) and CVD-mortality (0.91 [0.86–0.97]) after adjusting for MVPA. Joint models revealed that adults who met aerobic MVPA recommendations but did not weightlift had a 32% lower all-cause mortality risk (HR=0.68 [0.65–

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Author Contributions
JSG, BT and CEM contributed to the conception or design of the work. JSG drafted the manuscript. JSG, CEM, BT, and SCM contributed to the acquisition, analysis, or interpretation of data for the work. BT, CEM, ELW and SCM critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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The statements contained herein are solely those of the authors and do not represent or imply concurrence or endorsement by NCI.

Ethical Approval Information
The studies involving human participants were reviewed and approved by National Cancer Institute. The patients/participants provided their written informed consent to participate in this study.

Competing interests
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

0.70]), while those who also reported weightlifting 1–2x/week has a 41% lower risk (HR=0.59 [0.54–0.64]), both compared to adults reporting no aerobic MVPA or weightlifting. Without adjustment for MVPA, weightlifting was associated with lower cancer mortality (HR=0.85 [0.80–0.91]).

Conclusion: Weightlifting and MVPA were associated with lower risk of all-cause and CVD mortality, but not cancer mortality. Adults who met recommended amounts of both types of exercise appeared to gain additional benefit.

INTRODUCTION

Both aerobic and muscle strengthening physical activities are recommended for all adults to maximize health and increase longevity.[1] Aerobic physical activity is voluntary movement that increases energy expenditure above baseline levels and can be completed within the domains of transportation, leisure and recreation, or household activities of daily living. Muscle strengthening exercise (MSE) is defined as activities that increase or maintain muscular strength and endurance, balance, or body composition.[2] Weightlifting, whether using free weights or machines, is one of the most common types of MSE and has high recall validity as a self-reported exposure.[3] The 2018 Physical Activity Guidelines recommend all adults complete at least 150–300 minutes/week of moderate intensity aerobic physical activity, or 75–150 minutes/week of vigorous intensity aerobic activity or an equal combination of the two, commonly abbreviated as MVPA (moderate-vigorous physical activity). Importantly, all adults are also recommended to complete at least two days per week of MSE for all major muscle groups.[1,27] Recent prevalence estimates from the Behavioral Risk Factor Surveillance Survey (BRFSS) indicate approximately 65% of Americans met aerobic MVPA guidelines in 2015–2016.[4,5] Data from the National Health Interview Survey (NHIS) indicate approximately 28% of respondents reported sufficient MSE, and 24% of respondents met both the aerobic and MSE guidelines.[6]

While both aerobic MVPA and MSE are recommended for health benefits, most research has focused on aerobic MVPA.[2] Most evidence for the health benefits of MSE come from clinical studies with specific populations and short-term outcomes rather than from prospective observational studies with longer follow-up. Aerobic MVPA is consistently linked to lower mortality[7], however, few observational studies have examined the MSE-mortality association. Only 10 prospective epidemiologic studies have examined MSE and mortality yielding a mean risk reduction for any MSE (compared to none) of 20–25% for all-cause mortality.[8,9] A limitation of previous studies in MSE and mortality include the use of aggregated exposures (e.g., sessions/week, hours/week), which are often dichotomized into meeting/not meeting guidelines. This dichotomy, while sometimes useful, may obscure underlying dose-response associations between MSE and mortality. As such, the dose-response relationship between MSE and mortality has yet to be characterized fully including more detailed options of weightlifting frequency. Furthermore, the specific benefits of weightlifting on mortality are understudied, and important to examine with the popularity and specificity of weightlifting.

Given the few prospective observational studies and heterogenous assessments of MSE, the evidence base for weightlifting on mortality is quite limited. This study aimed to examine the relationship for weightlifting and all-cause mortality evaluating both independent and joint associations with aerobic MVPA. We also included cardiovascular disease (CVD) and cancer mortality analyses to examine common causes of death. We hypothesized that weightlifting would be associated with lower mortality

METHODS

Study population and patient involvement.

The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial was initiated in 1993 and includes 154,897 men and women aged 55–74 who were randomized into an intervention screening or control arm across ten different cancer centers in the United States including University of Colorado Health Sciences Center, Lombardi Cancer Research Center of Georgetown University, Pacific Health Research Institute, Henry Ford Health System, University of Minnesota School of Public Health/ Virginia L. Piper Cancer Institute, Washington University School of Medicine, University of Pittsburgh/Pittsburgh Cancer Institute/Magee-Women's Hospital, University of Utah School of Medicine, Marshfield (Wisconsin) Medical Research and Education Foundation, and the University of Alabama at Birmingham. In 2006 (13 years into the trial) follow-up questionnaires were sent to 104,002 participants. Many of those questions overlapped with the baseline questionnaire, however the follow-up questionnaire included information not captured at baseline including weightlifting. Cancer incidence and mortality of the cohort participants is updated regularly, with the most recent outcomes verified through December 2016. Ethical review was completed by National Cancer Institute and each of the 10 study sites. Informed consent was collected from all participants, the full trial details have been described elsewhere[10]. In this prospective cohort study for broad cancer screening, patients were not intimately involved in design or implementation of the trial or of these results.

Exposure assessment for weightlifting and aerobic MVPA.

The follow-up questionnaire had a specific prompt on weightlifting, asking if the participant had done any weightlifting in the past 12 months (less than once per month, one to three times per month, one to two times per week, three to six times per week, and seven or more times per week; see Supplemental material for copy of questionnaire). With these provided categorical response options, weightlifting was modeled as an ordinal categorical variable. Participants were not asked about weightlifting duration per session.

The follow-up questionnaire also asked about frequency and duration of physical activity in both moderate and strenuous intensity over the past year. Moderate intensity was prompted as "activity where you worked up a light sweat or increased your breathing and heart rate to moderately high levels". Adults reported the average days per week of moderate activity, as well as duration in category options of less than 15 minutes, 16–19 minutes, 20–29 minutes, 30–39 minutes, or 40 minutes or more. Strenuous activity was prompted as "activity strenuous enough to work up a sweat or increase your breathing and heart rate to very high levels" with the same response options as the moderate intensity, reported over the past year. Although the questionnaire prompted about "strenuous" activity, we will use the term vigorous for this investigation as the physiological cues about the intensity (sweating and breathing intensity) are consistent with vigorous intensity definitions, also "vigorous" aligns with the Physical Activity Guidelines for Americans. Using these frequency and duration estimates, four groups were generated based on total minutes of moderate- vigorous intensity activity (MVPA) including (1) inactive 0 minutes/week; (2) insufficient aerobic MVPA, 1–149 minutes/week; (3) meeting guidelines, 150–300 minutes/week moderate or an equivalent amount of vigorous activity; and (4) highly active, 301 or more minutes/week of moderate or an equivalent amount of vigorous activity.

Outcome assessment for mortality.

Mortality data was collected from annual study update questionnaires, reports from relatives and family members, from their physicians, or via linkage with the National Death Index (NDI). Once notification of a death occurred, PLCO screening centers acquired a death certificate. Primary and underlying causes of death were derived, coded, and recorded in PLCO databases. We evaluated death from any-cause as primary outcome (n=28,477 deaths). Additional outcomes included deaths from CVD (ICD-9 codes based on standard groupings for CVD, codes 200–400 (n=18,472) and cancer deaths (ICD-9 codes 100) (n=16,659). All-cause mortality was the primary outcome, we also included CVD- and cancer mortality analyses to examine associations with the most common causes of death.

Covariates.

Demographic and lifestyle covariates were selected from existing literature of mortality and weightlifting associaiotns[11–14]. All covariates were assessed at follow-up unless otherwise specified for time invariant variables (i.e., race and ethnicity, education, and sex). Questionnaires collected data on demographics, health behaviors including tobacco and alcohol use, personal health history, as well as self-reported height and weight.

Statistical analysis.

The following covariates were selected based on knowledge of the literature and directed acyclic graphs to select potential confounders. Variables included in the final regression model were: age (years); sex (male, female); education (<high school, high school graduate, some college, and college graduate +); body mass index (BMI) (<18.5, 18.6–24.9, 25–29.9, 30–34.9, 35+ kg/m^2), alcohol (grams/day, based on quartile distribution); self-reported race and ethnicity (Hispanic, non-Hispanic black, non-Hispanic white, and all other identities); smoking status (never, former, current); total number self-reported comorbidities from health history questionnaire (sum of arthritis, diabetes, emphysema, heart attack, hypertension, osteoporosis or stroke). Participants with missing data on physical activity were excluded from analysis (n=4,289).

Hazard ratios (HR) and 95% confidence intervals (CIs) for weightlifting and mortality were estimated using Cox proportional hazards regression with age as our time metric. For weightlifting and mortality risk analyses, those who reported no weightlifting in the last 30 days prior to follow-up questionnaire (non-weightlifters) were the reference group. Participants contributed person-time from completing the follow-up questionnaire until death (event) or the end of follow-up (censored, 2016) whichever came first. We used inverse probability selection weights (IPSW) to account for adults who did not consent for additional follow-up. The proportional hazards assumption was checked using visual inspection of the proportional hazards assumption, with no violations observed in the models for primary weightlifting exposures.

Spearman rank correlation coefficients were calculated across weightlifting and MVPA categories. We considered for main findings, HR and 95% CIs from the multivariate model, which provides information on the association between weightlifting and mortality, independent of confounders and MVPA. Weightlifting was modeled based on response options from the survey (no weightlifting, less than once per month, 1–3 times/month, 1–2 times/week, 3–6 times/week and 7+ times/week). However, due to the small number of deaths (n=198) in the highest weightlifting category (7+ times/week), the top two categories (3–6 times/week and 7+ times/week) of weightlifting frequency were combined. To estimate the direct (main) effect of weightlifting on mortality, models were run without adjustment for MVPA. Statistical models were also constructed to examine the independent influence of both activities (main effects) and separately conducted within groups of combined MVPA and weightlifting levels (joint effects). Stratified models were also constructed for further examination of main effects of weightlifting within aerobic MVPA strata.

Associations between weightlifting and cause-specific mortality (CVD, cancer) were calculated using Fine and Grey competing risks Cox regression[15]. We conducted two sensitivity analyses. The first was an evaluation of the primary weightlifting-mortality associations without adjustment for IPSW. Also, to evaluate potential reverse causality, all models were ran excluding deaths that occurred within the first two years of follow up.

Effect modification of the weightlifting-all cause-specific mortality association by age, sex, smoking, education, race, and BMI categories was evaluated using multiplicative interaction terms, with statistical significance assessed by Type III Wald test p value for the cross-product term. All statistical tests were two-sided, and p values of less than 0.05 were considered statistically significant; analyses were performed using SAS 9.4 (Cary, NC).

RESULTS

Demographics.

Of the 99,713 adults eligible for the current analysis, 28,477 deaths were observed over an average of 9.6 years of follow-up time. Mean age at the start of follow-up was 71.3 (Median 71, IQR 66–76) years, with mean BMI of 27.8 (Median 26.6, IQR 23.9–29.7) kg/m^2. Twenty-three percent of adults reported any weightlifting activity at follow-up and 16% of the sample reported weightlifting regularly between one to six times per week. Thirty two percent of the sample was sufficiently active, either meeting (23.6%) or exceeding (8.0%) the aerobic MVPA guidelines. Full demographic characteristics are presented by weightlifting responses in Table 1.

Correlation.

Spearman rank correlation coefficients between any weightlifting (binary yes/no) and aerobic MVPA categories were 0.28 ($p < 0.05$). Correlation between levels of weightlifting categories (frequency as reported) and aerobic MVPA categories were 0.27 ($p < 0.05$). Correlations between weightlifting and aerobic MVPA were not substantively different for men ($\rho = 0.27$, $p < 0.05$) or women ($\rho = 0.30$, $p < 0.05$).

Weightlifting and aerobic MVPA with and without mutual adjustment.

Overall, adults who reported any weightlifting had a 9% lower all-cause mortality risk (HR=0.91 [95%CI 0.88–0.94] Table 2) after adjustment for aerobic MVPA. Similar lower mortality risks were observed for CVD-mortality (HR=0.91 [0.86–0.97]) but not for cancer mortality. Adults who reported weightlifting 1–2 times/week had 14% lower all-cause mortality. MVPA-adjusted models revealed inverse trends between increasing categories of weightlifting and decreased risk of all-cause, CVD, and cancer mortality (all p for trend <.01). Adults who reported meeting the aerobic guideline had a 32% lower risk (HR=0.68 [0.65–0.70]) with mutual adjustment for weightlifting. Results presented are for the inverse probability selection weight adjusted models, and analyses with and without weighted adjustments yielded comparable results. Furthermore, sensitivity testing excluding deaths within the first two years did not yield appreciably different point estimates, therefore the results presented here are including all deaths in follow up.

Joint associations with weightlifting and aerobic MVPA.

Among non-weightlifters, any level of aerobic MVPA was associated with 24 to 36% lower all-cause mortality (e.g., HR meets=0.68 [0.65–0.70]) with reference group no MVPA and no weightlifting (Table 3). Among adults reporting no aerobic MVPA, any weightlifting was associated with 9 to 22% lower mortality (e.g., 1–2 times/week, HR=0.80 [0.71–0.92]). Notably, compared to adults with neither MVPA or nor weightlifting, those who reported both types of exercise tended to have lower mortality than either exercise behavior alone. For example, adults who reported at least recommended MVPA levels with weightlifting 1–2 times/week had 41 to 47% lower risk (e.g., meets aerobic and 1–2x/week HR=0.59 [0.54–0.60]), compared to the common reference group of no aerobic or weightlifting exercise. This finding suggests that both types of exercise have an additive mortality benefit.

Weightlifting stratified by aerobic MVPA.

Stratified analyses are presented as supplemental material (Supplemental Table 2). When restricting analyses within strata of aerobic MVPA (none, some, meets, exceeds), inverse all-cause mortality hazard reductions were observed for unit increase of weightlifting (HR 0.98, 0.97, 0.98, 0.95, respectively).

Effect modification.

Education, smoking, BMI, race, and ethnicity did not significantly modify the weightlifting-all-cause mortality associations. We did find statistical evidence for heterogeneity by sex indicating a stronger association of weightlifting and mortality in women (Table 5).

DISCUSSION

In this large cancer screening trial, consistent independent and joint weightlifting mortality reductions were observed. Weightlifting and aerobic MVPA were both independently associated with lower all-cause and CVD mortality. However, lower risk was not apparent for cancer mortality. Observed associations between weightlifting and all-cause mortality did not appear to vary by the participant factors we examined other than sex. We found statistical evidence that the weightlifting-all-cause mortality association was stronger in women. Joint models revealed 32% lower all-cause mortality with meeting aerobic MVPA guidelines without any weightlifting, conversely weightlifting 1–2x/week was associated with 20% lower all-cause mortality without any aerobic MVPA. Reporting both MVPA and weightlifting together were associated with a 41% lower all-cause mortality. In joint models, our data show that weightlifting with most levels of aerobic MVPA was associated with 15–47% lower all-cause mortality.

While we focused on weightlifting, a type of MSE, ten prospective observational studies have examined the MSE-mortality association. Five publications were able to categorize respondents into those meeting MSE guidelines of at least 2 sessions/week, often revealing a lower mortality with MSE.[16–20] Other studies were able to dichotomize into those who report any (vs. those who do not) MSE[21,22], and other studies used total duration (instead of frequency) of muscle strengthening activity.[23–25] Prospective investigations using duration exposures (e.g., hours/week) for MSE are difficult to translate into meeting the physical activity guidelines since those are delivered in session frequency, not duration. Our results are specific to weightlifting and may not fully capture all MSE which prevented us from categorizing our results into meeting MSE guidelines. Furthermore, the questionnaire response options from the PLCO cohort do not map exactly on to the two sessions per week option (i.e., options of 1–2 sessions/week and 3–6 sessions/week). Of previously published studies, none exclusively used weightlifting as the exposure. Six studies[17,18,20,23–25] used prompts on weightlifting with strength training as MSE assessments, whereas four studies[16,19,21,22] used a broader definition of muscle strengthening activities or strength promoting exercise. Our study adds knowledge on weightlifting exercise, but we recognize that it is not the only modality of MSE which may also include calisthenics, Pilates, and plyometrics. Our findings support the joint mortality benefits of MSE (via weightlifting) along with aerobic activity, in amounts that approximate current physical activity guidelines[1,27] although we were unable to explicitly test the two session/week recommendation directly.

There are several potential pathways by which weightlifting could be associated with mortality, including the influence of weightlifting on body composition leading to more lean mass and thus improved function.[28] Total lean mass is also independently associated with lower mortality risk, with studies examining the muscle’s role in both endocrine and paracrine functions, and thus how that can influence health.[29] Finally, weightlifting in particular could be a socially-related behavior in that those who weightlift participate in social networks, assuming that this behavior is done in a gym with others.[30] However, it is important to acknowledge that consistent weightlifting is associated with other improvements including functional strength gains and improved musculoskeletal health.[26]

These are hypothesized mechanisms, due to the nature of this study we cannot fully examine these potential relationships.

Our study has limitations including that this is a single observational study which cannot alone establish causality but still adds value to the totality of the evidence base. There may be measurement error associated with recall of weightlifting behavior, however self-reported recall is an appropriate assessment technique for prospective observational studies.[3] Our study has a single time assessment of a time-varying behavior, which is a limitation. We did not have repeated measures to capture changes in behavior over time, thus serial measurement with longer follow up time in future studies would be informative. This analysis was limited by the lack of specific details about weightlifting that could be informative for a dose-response investigation including training intensity, training load, volume (set and reps), and for how long the adult has been participating in weightlifting. Given the exposure categories provided we are unable to perfectly harmonize weightlifting frequency of at least two days per week from the Physical Activity Guidelines. We had limited observations for the highest level of weightlifting frequency (7+ days/week) and mortality, therefore we combined categories to ensure we had appropriate statistical power. Finally, this study might not be generalizable to other racial and ethnic groups or younger study populations given that the PLCO study population was predominantly non-Hispanic White with mean age of 71 years at follow-up questionnaire assessment. Strengths of our investigation include the size of the population and the unique exposure and frequency assessment of weightlifting. The cohort updates the cancer incidence and mortality data regularly which allows for cancer mortality for independent and joint associations of weightlifting and MVPA. Our analysis used inverse probability selection weights to combat losses to follow-up including those who did not consent to the follow-up questionnaire. Our sensitivity analyses restricting to those who died after the first two years of follow did not change our results, which lowers the potential for confounding by poor health status. Finally, our results are generalizable to a primarily non-Hispanic White, older adult population demonstrating the beneficial weightlifting-mortality association.

In conclusion, participants who engaged in weightlifting had a lower risk of mortality after accounting for aerobic MVPA, and the combination of weightlifting and aerobic MVPA provided more benefit than either type of exercise alone. Our study provides support for weightlifting as a health behavior associated with longevity for older adults at varying levels of aerobic MVPA participation. Importantly, these findings support meeting both the aerobic MVPA and muscle strengthening (including weightlifting) recommendations, especially targeting older adults who do not weightlift but may be currently aerobically active to maximize health and mortality outcomes. Future studies are needed to more clearly define the MSE-mortality dose-response relationship and to better understand if the associations observed in the present report hold in diverse populations. Additionally, future work should include more precise estimates of MSE (including weightlifting) to include both frequency, intensity and duration estimates to improve our understanding of the dose-response relationship for mortality and other health-related outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Sharing Statement

Publicly available datasets were analyzed in this study. This data can be found here: https://cdas.cancer.gov/datasets/plco/.

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What is already known on the topic?

- Aerobic activity has consistently shown to be associated with lower mortality, but the relationship for weightlifting behavior independently and together with MVPA on mortality outcomes is less understood

What this study adds?

- MVPA-adjusted models revealed inverse trends between increasing categories of weightlifting and decreased risk of all-cause, CVD, and cancer mortality (all p for trend <.01).
- Weightlifting in older adults was independently associated with lower all-cause and CVD mortality, and only associated with cancer mortality without adjustment for MVPA
- Among adults reporting no aerobic MVPA, any weightlifting was associated with 9 to 22% lower all-cause mortality
- Lower all-cause mortality was observed in older adults doing either aerobic or weightlifting exercise, but the lowest mortality risk was observed among adults who reported both types of exercise.

How this study might affect research, practice, or policy?

- Our finding that mortality risk appeared to be lowest for those who participated in both types of exercise provides strong support for current recommendations to engage in both aerobic and muscle strengthening activities.
- The weightlifting-associated mortality benefit shown here provides initial evidence to clinicians and other health professionals that older adults would likely benefit from adding weightlifting exercises to their physical activity routines.

Table 1:

Study sample demographics by levels of weightlifting as reported.

	None n=75069 (76.8%)	Less than 1 times/month n= 1436 (1.5%)	1–3 times/ month n=4146 (4.2%)	1–2 times/week n=8311 (8.5%)	3–6 times/ week[1] n=8224 (8.4%)	7 or more[1] times/week n=584 (0.6%)
Age at randomize	62.3 (5.2)	60.6 (4.8)	60.8 (4.8)	61.1 (4.9)	61.6 (4.9)	63.2 (5.3)
Age at follow up	71.4 (5.9)	69.5 (5.7)	69.8 (5.6)	70.2 (5.7)	70.8 (5.6)	72.6 (6.2)
# comorbidities	1.3 (1.2)	1.1 (1.2)	1.1 (1.1)	1.0 (1.1)	1.0 (1.1)	1.2 (1.2)
BMI[2] (kg/m^2)						
<18.5	2956 (3.9%)	56 (3.9%)	147 (3.6%)	312 (3.8%)	312 (3.8%)	34 (5.8%)
18.5–24.9	22804 (30.4%)	488 (34.0%)	1593 (38.4%)	3509 (42.2%)	3505 (42.6%)	245 (41.9%)
25–29.9	31391 (41.8%)	635 (44.2%)	1710 (41.2%)	3299 (39.7%)	3235 (39.3%)	211 (36.1%)
30–34.9	12706 (16.9%)	193 (13.4%)	522 (12.6%)	927 (11.1%)	936 (11.4%)	73 (12.5%)
35+	5212 (6.9%)	64 (4.5%)	174 (4.2%)	264 (3.2%)	236 (2.9%)	21 (3.6%)
Sex						
Men	35737 (46.8%)	654 (45.0%)	1938 (46.1%)	3847 (45.6%)	4604 (55.1%)	347 (58.9%)
Women	40691 (53.2%)	800 (55.0%)	2270 (53.9%)	4594 (54.4%)	3755 (44.9%)	242 (41.1%)
Race						
White	68447 (91.4%)	1292 (91.0%)	3767 (91.2%)	7644 (92.5%)	7495 (91.3%)	526 (91.3%)
Black	2474 (3.3%)	49 (3.5%)	115 (2.8%)	183 (2.2%)	158 (1.9%)	13 (2.3%)
Hispanic	1073 (1.4%)	26 (1.8%)	73 (1.8%)	115 (1.4%)	175 (2.1%)	15 (2.6%)
Other	2914 (3.9%)	53 (3.7%)	176 (4.3%)	325 (3.9%)	385 (4.7%)	22 (3.8%)
Smoking						
Never	35309 (46.9%)	652 (45.5%)	1935 (46.7%)	3813 (45.7%)	3649 (44.2%)	292 (50.1%)
Former	544 (7.4%)	63 (4.4%)	183 (4.4%)	308 (3.7%)	323 (3.9%)	22 (3.8%)
Current	34386 (45.7%)	717 (50.0%)	2023 (48.9%)	4218 (50.6%)	4286 (51.9%)	269 (46.1%)
Alcohol intake						
None	28 (0.1%)	0 (0%)	2 (0.1%)	3 (0.1%)	3 (0.1%)	0 (0%)
<0.2 g/day	8703 (25.6%)	127 (20%)	371 (19.9%)	688 (18.3%)	688 (18.8%)	69 (24.5%)
0.2–1.39 g/day	8388 (24.6%)	143 (22.5%)	422 (22.6%)	774 (20.6%)	793 (21.7%)	69 (25.5%)
1.4–10.7 g/day	8725 (25.6%)	181 (28.5%)	508 (27.3%)	1102 (29.4%)	1009 (27.6%)	61 (22.5%)
10.7 g/day +	8209 (24.1%)	184 (29.0%)	561 (30.1%)	1185 (31.6%)	1170 (31.9%)	72 (26.6%)
Education						
<High School	4445 (5.9%)	19 (1.3%)	82 (2.0%)	161 (2.0%)	226 (2.8%)	39 (6.8%)
High School	18400 (24.6%)	176 (12.4%)	585 (14.2%)	1113 (13.5%)	1258 (15.4%)	105 (18.3%)
College	26250 (35.1%)	444 (31.3%)	1345 (32.6%)	2633 (31.9%)	2579 (31.5%)	188 (32.8%)
College +	25653 (34.3%)	779 (54.9%)	2114 (51.2%)	4346 (52.7%)	4134 (50.4%)	242 (42.2%)

	None n=75069 (76.8%)	Less than 1 times/month n= 1436 (1.5%)	1–3 times/ month n=4146 (4.2%)	1–2 times/week n=8311 (8.5%)	3–6 times/ week[1] n=8224 (8.4%)	7 or more[1] times/week n=584 (0.6%)
Aerobic MVPA groups						
None (0 mins)	27792 (36.7%)	466 (32.2%)	881 (21.1%)	757 (9.0%)	509 (6.1%)	76 (13.0%)
Some (1–149 mins)	27871 (36.8%)	592 (40.9%)	1923 (46.0%)	3603 (48.9%)	2416 (29.1%)	144 (24.5%)
Meets (150–300 mins)	15173 (20.1%)	326 (22.5%)	1096 (26.2%)	3261 (38.9%)	3553 (42.8%)	171 (29.1%)
Exceeds (301+ mins)	4847 (6.4%)	64 (4.4%)	284 (6.8%)	780 (9.3%)	1834 (22.1%)	196 (33.4%)

[1]For regression analysis, these top two categories were combined of 3–6 times/week and 7+ per week due to the small number of deaths in these categories.

[2]BMI abbreviates Body Mass Index

Table 2.

Muscle strengthening and aerobic exercise associated with all-cause and cause-specific mortality with and without mutual adjustment

(HR and 95% CIs). Weighted estimates to the whole cohort are presented.

		All-cause mortality HR (95%CI)		CVD mortality HR (95%CI)		Cancer mortality HR (95%CI)	
	Deaths (n)	**Model A**	**Model A + MVPA[1]**	**Model A**	**Model A + MVPA**	**Model A**	**Model A + MVPA**
Weightlifting Yes (vs. no)	3,835	0.79 (0.76–0.81)	0.91 (0.88–0.94)	0.76 (0.76–0.80)	0.91 (0.86–0.97)	0.85 (0.80–0.91)	0.96 (0.90–1.02)
Weightlifting frequency							
Never	22,086	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Less than once/month	300	0.82 (0.74–0.92)	0.84 (0.76–0.94)	0.84 (0.70–1.03)	0.86 (0.71–1.05)	0.88 (0.72–1.07)	0.91 (0.75–1.11)
One to three times/month	874	0.80 (0.75–0.85)	0.85 (0.79–0.91)	0.82 (0.73–0.92)	0.89 (0.79–0.99)	0.80 (0.71–0.90)	0.85 (0.75–0.96)
One to two times/week	1,712	0.76 (0.73–0.80)	0.86 (0.82–0.91)	0.73 (0.97–0.79)	0.85 (0.78–0.93)	0.88 (0.81–0.96)	0.97 (0.89–1.06)
Three to 7+ times/week	2,123	0.79 (0.75–0.82)	0.93 (0.89–0.98)	0.76 (0.71–0.82)	0.95 (0.88–1.03)	0.81 (0.75–0.88)	0.93 (0.85–1.01)
Per unit increase in weightlifting category		0.93 (0.92–0.94)	0.97 (0.96–0.98)	0.92 (0.91–0.94)	0.97 (0.96–0.99)	0.95 (0.93–0.96)	0.98 (0.96–0.99)
P for trend		<.0001	<.0001	<.0001	0.002	<.0001	0.03
MVPA groups							
None	11,203		1.00 (ref)		1.00 (ref)		1.00 (ref)
Some	9,574		0.76 (0.74–0.78)		0.73 (0.69–0.77)		0.78 (0.74–0.82)
Meets	5,365		0.68 (0.65–0.70)		0.65 (0.62–0.69)		0.70 (0.66–0.75)
Exceeds	1,788		0.66 (0.63–0.70)		0.65 (0.60–0.71)		0.70 (0.64–0.77)

Model A adjusted for age at follow-up questionnaire, sex, education, smoking, alcohol intake, current BMI category, race, and number of comorbidities.

[1]MVPA abbreviates moderate to vigorous physical activity, these results include covariates from Model A plus each group of aerobic activity guidelines (inactive 0 minutes of activity, insufficient of 1–149 minutes of activity, meets guidelines 150–300 minutes of activity, highly active of 301+ minutes of activity).

Table R1.

Cross frequency of adults within each aerobic physical activity and weightlifting levels.

Total number (n) and percent sample (%) presented, with total number of deaths per cell.

Weightlifting frequency	No MVPA[1]	Some MVPA	Meets MVPA	Exceeds MVPA
Never	27792 (17.9%) 9918	27871 (18.0%) 7245	15173 (9.8%) 3540	4847 (3.1%) 1114
Less than once/month	466 (0.3%) 125	592 (0.4%) 106	326 (0.2%) 59	64 (0.04%) 8
One to three times/month	881 (0.6%) 247	1923 (1.2%) 381	1096 (0.7%) 197	284 (0.2%) 41
One to two times/week	757 (0.3%) 226	3603 (1.6%) 780	3261 (2.3%) 579	780 (1.2%) 116
Three to 6 times/week	509 (0.3%) 177	2416 (1.6%) 634	3553 (2.3%) 721	1834 (1.2%) 385
7+ times/week	76 (0.05%) 35	144 (0.09%) 60	171 (0.1%) 52	196 (0.1%) 51

[1]Abbreviates moderate to vigorous physical activity (MVPA).

Table 3.

Joint models of aerobic activity and weightlifting for all-cause mortality risk. Hazard ratios (HR) and 95% confidence intervals are presented, weighted estimates to the whole cohort.

		Aerobic activity			
		No MVPA	**Some MVPA**	**Meets MVPA**	**Exceeds MVPA**
Weightlifting	None	1.00 *reference*	0.76 (0.73–0.78)	0.68 (0.65–0.70)	0.66 (0.62–0.70)
	<1x/month	0.78 (0.66–0.93)	0.65 (0.54–0.78)	0.67 (0.52–0.85)	0.51 (0.27–0.99)
	1–3x/month	0.85 (0.75–0.97)	0.65 (0.59–0.72)	0.56 (0.49–0.62)	0.55 (0.41–0.74)
	1–2x/week	0.80 (0.71–0.92)	0.67 (0.63–0.72)	0.59 (0.54–0.64)	0.53 (0.44–0.63)
	3–7+x/week	0.91 (0.80–1.04)	0.73 (0.68–0.79)	0.61 (0.57–0.65)	0.63 (0.57–0.69)

Models adjusted for age at questionnaire (where weightlifting was assessed), sex, education, smoking, alcohol intake, current BMI, race, and number of comorbidities. Aerobic moderate to vigorous physical activity (MVPA) categories are none (0 minutes per week), some (1–149 minutes/week), meets (150–300 minutes/week) and exceeds (301+ minutes/week). *p* value for the weightlifting*aerobic activity term was 0.69.

Table 5.

Effect modification of the weightlifting (yes, no) all-cause mortality association by strata of relevant covariates.[1]

Covariate stratification Hazard ratio [95% confidence interval]	*P value interaction term*
Age Under 71 years: 1.08 [1.07–1.09) Older than, including 71: 1.11 [1.11, 1.12]	0.85
Sex Men: 0.96 [0.90–1.03] Women: 0.82 [0.75–0.90]	0.001
Smoking Never: 0.88 [0.91–0.95] Current: 0.95 [0.89–1.03]	0.50
Self-reported racial identity White: 0.91 [0.86–0.96] Non-white: 0.81 [0.65–1.02]	0.06
Education No college: 0.91 [0.84–0.98] College plus: 0.93 [0.89–0.97]	0.79
Body Mass Index <24.9 kg/m2: 0.77 [0.50–1.12] 25–29.9 kg/m2: 0.97 [0.90–1.06] 30.0+ kg/m2: 0.84 [0.73–0.97]	0.31

[1]Hazard ratios and 95% confidence intervals are presented, weighted estimates to the whole cohort.